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SEROPROPHYLAXIS IN EXPERIMENTAL RABIES [1]

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It is the opinion of most workers in the field of virus diseases that the effectiveness of immune serum ceases once the virus has entered the susceptible cell. Therefore, from the practical viewpoint its use is largely limited to those instances where the time of exposure is known.

Rabies is a virus disease peculiar in two respects: first, because the time of exposure is usually definitely known, and secondly, because the incubation period is often sufficiently prolonged so that an active immunity can be produced before the virus has established itself in the vital centers of the central nervous system.

Theoretically then, because of the known exposure and prolonged incubation period, seroprophylaxis in rabies should be highly effective, provided protection is in part or entirely due to circulating antibodies. However, relatively little consideration has been given to this method of prevention in this country.

Following Babes and Lepp's (*1*) first preparation of immune rabies serum many experiments were published on the prevention of rabies in animals by the use of immune serum given by various routes both before and after infection (*2, 3, 4, 5, 6, 7, 8, 9, 10*). All of these experiments were based on only a few animals and were inadequately controlled, and the results varied from complete protection (Fermi (*7*)) to no protection (Marie (*10*)).

Later Proca, Babes, and Jonnesco, in a series of publications (*11, 12, 13, 14, 15*), presented experimental evidence in guinea pigs and rabbits that, following peripherally inoculated fixed and street virus, serum given locally at the site of virus introduction or subcutaneously would prevent rabies. All of their experiments, however, involved small numbers of animals and large doses of serum and the difference

[1] From the Division of Infectious Diseases, National Institute of Health.

between control and treated groups frequently was not great. These same workers also reported on the use of serum alone and combined with vaccine in man as follows:

1934. 40 cases bitten on face and treated with serum with 1 death (2.5 percent); 47 cases bitten on face and treated with vaccine, with 4 deaths (8 percent).
1935. 179 cases treated with serum and vaccine, with 4 deaths (2.2 percent).
1936. 163 cases treated with serum and vaccine, with 5 deaths (3 percent).

They recommended 80 to 160 cc. of subcutaneously administered serum as giving best results in man.

British workers in India (*16*, *17*, *18*) have done experimental work in monkeys and have attempted the practical application of seroprophylaxis in man. In two of four adequately controlled monkey experiments they were able to show that serum given on the first and second days following virus inoculation, together with the usual course of vaccine, gave significantly better results than either serum or vaccine alone. In humans, using 20 cc. of serum on the first day and the same dose on the second day, together with a full course of vaccine in alternate class IV (severe bites on head or neck) cases as compared to vaccine alone, the results were:

1935. Serum and vaccine—1,028 cases treated, with 20 deaths (1.9 percent).
Vaccine alone—340 cases treated, with 9 deaths (2.5 percent).
1936. Serum and vaccine—948 cases treated, with 16 deaths (1.6 percent).
Vaccine alone—1,475 cases treated, with 33 deaths (2.2 percent).

The serum used in these British studies was produced in sheep by a long series of large doses of killed and live virus vaccines. The only tests made of serum potency were by complement fixation. An attempt was made to concentrate the rabies immune antibody by ammonium sulfate fractional precipitation. These workers concluded that the antibody was in the euglobulin fraction.

Hoyt et al. (*19*, *20*, *21*, *22*) in this country, using fixed and street viruses in mice and immune rabbit serums, have shown that serum, to be effective, must be given 24 to 48 hours before virus, if the mice are injected intracerebrally, but that protection is also afforded after inoculation if the virus is given peripherally.

In the most recent contribution to seroprophylaxis of rabies, Yen (*23*) has worked with fixed virus intramuscularly in mice. Employing serial virus and serum dilutions he has established a quantitative method of testing the potency of antirabies immune serum.

METHODS EMPLOYED IN PRESENT STUDY

COMPARATIVE TESTS IN ANIMALS (PROPHYLAXIS)

Guinea pig tests.—In our work guinea pigs weighing from 250 to 300 gm. were inoculated into the masseter muscle with 0.25 cc. of a

heavy emulsion (usually 20-percent emulsion supernatant) of first passage guinea pig brain street virus.[2]

The prophylactic treatment was begun at varying intervals following the injection of street virus. Guinea pigs were checked daily for symptoms and when death occurred the brain was examined for Negri bodies. If the brain was Negri negative, Ammon's horn and medulla were emulsified and injected intracerebrally into 4-week-old Swiss mice for confirmation. Mice were observed for 30 days.

All guinea pigs were observed for 2 to 3 months before being discharged.

Mouse tests.—Swiss mice, 1 month of age, were inoculated in the gastrocnemius muscle with 0.03 cc. of either a fixed dilution or serial dilutions of an intramuscular strain of fixed virus. At various intervals the prophylactic inoculations of serum, of vaccine, or of both were begun, the material being given by different routes. All mice were observed for 30 days and only those with typical hind-leg paralysis preceding death were diagnosed as rabies.

Monkey tests.—Street virus after one passage in monkeys was inoculated into the masseter muscle. Treatment was instituted 24 hours after virus inoculations, the doses of serum and vaccine being the same as for humans. Brains of all animals killed, with symptoms or dying, were examined for Negri bodies and as a check portions of the medulla and Ammon's horn were emulsified and inoculated into mice whose brains also were checked for Negri bodies during symptoms or after death. Susceptibility of monkeys to street virus by the intramuscular route varied with body weight so that weights were equalized within all groups on each experiment.

VIRUS NEUTRALIZATION TEST (IN VITRO NEUTRALIZATION OF VIRUS)

Mouse brain fixed virus was made up in a 20-percent emulsion and serial tenfold dilutions made in buffered salt solution from the centrifuged supernatant. Two-tenth of a cubic centimeter of each virus dilution was mixed with 0.2 cc. of undiluted serum, incubated for 1 hour at 37° C., then inoculated intracerebrally into 1-month-old Swiss mice. Fifty percent end points were determined.

VIRUS PROTECTION TEST (IN VIVO NEUTRALIZATION OF VIRUS)

Brains of mice inoculated intramuscularly with the Rockefeller 15811 strain[3] were made to a 1/4 emulsion. Serial twofold dilutions of the supernatant made in buffered salt solution were inoculated into the gastrocnemius muscle of 1-month-old Swiss mice, 0.03 cc.

[2] Street virus dog brains kindly supplied by Dr. C. N. Leach and Dr. Harald Johnson of the Rockefeller Field Rabies Laboratory.

[3] Kindly supplied by Dr. L. T. Webster of Rockefeller Institute for Medical Research.

to the dose. Immediately after the virus inoculation 0.2 cc. of serum was injected intraperitoneally or subcutaneously. Rabies in mice receiving this virus strain in the gastrocnemius muscle almost invariably is preceded by paralysis of one or both hind legs. Fifty percent end points were determined.

COMPLEMENT FIXATION TEST

The technique of Casals and Palacios (*24*) was followed with the exception that fixation was allowed to take place at 37° C. for 1 hour instead of overnight in the ice box. The usual serum and antigen controls were included in each test and all serums being compared were run in a single test. All serums having a titer of 1/64 or over were rechecked. A 2+ fixation was taken as the end point.

PRODUCTION OF IMMUNE RABBIT SERUMS

Three groups of rabbits were inoculated. The first group received the supernatant prepared by the horizontal centrifuging at 1,000 r. p. m. for 10 minutes of a 10-percent emulsion of mouse-brain fixed virus. The second group received the supernatant of the same virus emulsion after angle centrifuging at 4,000 r. p. m. for 30 minutes. The third group received a 10-percent whole emulsion of the mouse-brain virus. Doses were started at 0.25 to 0.5 cc. and brought up to a maximum of 3 cc. The routes of inoculation and time intervals between doses varied in different groups. When given intracutaneously 0.5 cc. was injected into each site. All bleedings were done from 10 to 14 days following the last dose of virus.

CONCENTRATION OF SERUM

Pooled rabbit serums were heated to 40° C. and anhydrous sodium sulfate added in varying amounts (*25*). After heating at 37° C. for several hours it was then angle centrifuged. The precipitate was placed in cellophane tubing and dialyzed overnight against running tap water. The dialyzed serum was adjusted to various fractions of its original volume and filtered through a Berkefeld N filter.

VACCINE POTENCY TEST

Vaccine was diluted to 0.5-percent emulsion and 0.25 cc. given intraperitoneally every 2 days for six doses to fifty 1-month-old Swiss mice. Fourteen days from the first dose of vaccine the test dose of fixed virus was given intracerebrally in serial tenfold dilutions. Control mice were included for titering the 50-percent end point of the test virus and results expressed in the number of 50-percent end point MLD against which the vaccinated mice were protected (*26*).

PRODUCTION OF SERUM

In determining the best schedule of inoculation of virus for the production of immune serum in rabbits, several items of practical importance must be considered, namely, the rapidity of formation, the quality and the persistence of antibody, the ease of administration, and the mortality rate due to the procedure.

From tables 1 and 2 it can be seen that intracutaneously inoculated virus gave the highest protective antibody titers; the antibody titer reached a peak at 11 weeks and was maintained during continuing inoculations. Titers dropped soon after inoculations were discontinued but increased again after two restimulating doses of virus. Two doses a week of virus intracutaneously gave a better response than one weekly dose.

TABLE 1.—*Serum antibody response in rabbits, by routes of virus inoculation*

Route of virus inoculation	Number inoculated	Death during inoculation	Method of testing	Results					
				Before immunization	After immunization (days)				
					27	56	81	119	145
Subcutaneous [1]	6	2 (rabies)	Virus neutralization [2]	0	--------	100	10,000	1,000	10,000
			Complement fixation	0	--------	1/16	1/32	1/16	1/16
			Virus protection [2]	10	27	15	50	25	35
Intraperitoneal [1]	6	1 (rabies)	Virus neutralization [2]	0	100	100	1,000	1,000	10,000
			Complement fixation	0	1/512	1/256	1/512+	1/64	1/32
			Virus protection [2]	10	34	34	30	40	50
Intracutaneous [1]	6	0	Virus neutralization [2]	0	10,000+	10,000	10,000	10,000+	10,000
			Complement fixation	0	1/64	1/64	1/32	1/64	1/32
			Virus protection [2]	10	74	64	75	85	80
Intravenous [1]	6	1 (rabies)	Virus neutralization [2]	0	100	100	--------	--------	------
		5 (shock)	Complement fixation	0	1/512	1/512	--------	--------	------
			Virus protection [2]	10	29	44	--------	--------	------

[1] 10 percent mouse brain rabies fixed virus supernatant 0.5-cc., 1.0-cc., 2.0-cc., 3.0-cc. doses weekly.
[2] Minimum lethal doses in mice.

TABLE 2.—*Serum protective antibody response in rabbits. Effect of interval of dose and restimulating dose of virus on height and persistence of antibody*

Schedule of intracutaneous inoculation of virus [1]	Continuous inoculation (time bled, in weeks)					Time after last inoculation (weeks)		After 1 restimulating dose	After 2 restimulating doses
	5	11	17	23	29	4	6		
	MLD								
3 cc. weekly	18	23	9	15	10	5	6	6	25
1.5 cc. weekly	9	42	20	19	15	--------	--------	--------	--------

[1] 10 percent whole emulsion rabies mouse brain fixed virus.

CONCENTRATION OF SERUM

By fractional sodium sulfate precipitation of the complement fixing and the protective antibody from rabies immune rabbit serum all demonstrable antibody of both types was found to be precipitated by 16 percent sodium sulfate.

GUINEA PIG EXPERIMENTS

DOSE OF IMMUNE SERUM

Thirty-five guinea pigs were inoculated in the right masseter muscle with 0.25 cc. of 1/6 supernatant of first guinea pig passage brain street virus. Five additional guinea pigs received the same dose of a 1/600 dilution of the same supernatant. Three hours later unconcentrated immune rabbit serum was given subcutaneously to groups of 10 guinea pigs in doses of 0.5 cc., 2.0 cc., and 5.0 cc., respectively.

Table 3 reveals that guinea pigs receiving 0.5 cc. of serum had a mortality of 12 percent; those receiving 2.0 cc. of serum, 28 percent mortality; all receiving 5.0 cc. of serum survived; there was 100 percent mortality of the controls. Two out of five controls receiving 1/600 of the test dose died of rabies.

TABLE 3.—*Serum prophylaxis of rabies in guinea pigs. Effect of dose*

	Number of guinea pigs	Deaths	
		Rabies	Nonrabies
Dose of serum subcutaneously:[1]			
0.5 cc.	10	1	2
2.0 cc.	10	2	3
5.0 cc.	10	0	1
Controls:			
1/6 dilution	5	5	0
1/600 dilution	5	2	0

[1] Serum administered 3 hours after 0.25 cc. of 1/6 supernatant of first guinea pig passage street virus in masseter muscle.

The immune rabbit serum used in this experiment had a virus neutralizing titer in mice of 1,000 MLD per 0.03 cc.

COMPARISON OF SERUM AND VACCINE PROPHYLAXIS

Tables 4, 5, and 6 show the results of four tests in which groups of guinea pigs were inoculated in the masseter muscle with early passage street virus followed by unconcentrated serum, by vaccine, or by a combination of the two administered after various intervals.

The serum used in these experiments was administered subcutaneously. Different types of vaccine were used and in tables 4, 5, and 6 is indicated the potency of each vaccine by the mouse test insofar as it was determined.

Table 4 shows a direct comparison of serum alone and vaccine alone when prophylactic therapy was begun at intervals of 3, 24, and 48 hours after the injection of virus. The mortality in serum-treated animals was 11, 33, and 60 percent, and for vaccine-treated animals 80, 100, and 83 percent as the time intervals increased. Thus there was a definite difference in favor of the serum-treated group. This

difference is further brought out by comparing the average time of deaths in the two groups. The relatively large number of nonrabies deaths in the vaccine-treated groups must be considered in interpreting these results.

TABLE 4.—*Serum vs. vaccine prophylaxis of rabies in guinea pigs. Treatment administered at varying intervals after virus inoculation*

Treatment	Time from virus inoculation [3] to treatment (hours)	Number of guinea pigs	Deaths		Average time of survival (days)
			Rabies	Nonrabies	
2 cc. serum subcutaneously [1]	3	10	1	1	28
Do	24	10	3	1	34
Do	48	10	6	0	47
Vaccine [2]	3	10	4	5	13
Do	24	10	3	7	14
Do	48	10	5	4	13
Controls		5	5	0	16

[1] 1 dose unconcentrated rabbit immune serum.
[2] 2 cc. 5-percent phenolized vaccine subcutaneously daily for 10 doses. Vaccine potency 1,000 MLD.
[3] 0.25 cc. of 1/5 supernatant dog brain street virus in masseter muscle.

In table 5 is shown an attempt to include a combination of serum and vaccine therapy in the comparative testing. All therapy was started 24 hours after the virus had been injected. In group 3 the course of vaccine was commenced on the same day that serum was administered, whereas in group 4 an interval of 4 days was allowed before starting vaccine but only one dose of serum was given in both groups. There was a moderate degree of protection with serum alone,

TABLE 5.—*Serum and vaccine, alone and combined, in rabies prophylaxis in guinea pigs*

Treatment [1]	Number of guinea pigs	Number of deaths		Average time of survival (days)
		Rabies	Nonrabies	
Serum [2]	10	6	1	14
Vaccine [3]	10	9	1	11
Serum, with vaccine started same day as serum	10	3	0	14
Serum, with vaccine started 4 days after serum	10	1	0	12
Controls	10	9	0	12

[1] All treatment started 24 hours after 0.25 cc. 1/5 supernatant of first guinea pig passage street virus in masseter muscle.
[2] 1 dose of 1 cc. of unconcentrated rabbit immune serum subcutaneously.
[3] 0.1 cc. subcutaneously daily for 21 days of 5-percent phenolized vaccine—vaccine potency 56 MLD.

none with vaccine alone, good protection when serum and vaccine were started the same day, and only 1 out of 10 died of rabies when 4 days elapsed between serum and vaccine treatment. Obviously the vaccine used in this experiment was a poor one (potency 56 MLD), yet its use in combination with serum was followed by a definite lowering of the mortality.

The same comparisons as in the previous test are shown in table 6 but here a potent vaccine was used and therapy was started at intervals of 3 and 72 hours after the virus injections. A further comparison was also made in which vaccine therapy was not begun until 6 or 7 days after serum had been administered. This experiment was done in two parts on 2 different days. The serum and vaccine used in both were the same. The test virus emulsion was kept frozen at −70° C. between tests yet there was a difference of between

TABLE 6.—*Serum and vaccine, alone and combined, in rabies prophylaxis in guinea pigs. Treatment started at varying intervals after virus inoculation*

Treatment	Time from virus inoculation [1] to treatment (hours)	Number of guinea pigs	Number of deaths		Average time of survival (days)
			Rabies	Nonrabies	
Vaccine [2]	0	10	6	0	13
Serum [3]	0	10	5	1	33
Serum, with vaccine started same day as serum	0	10	3	0	25
Serum, with vaccine started 3 days after serum	0	10	4	1	34
Serum, with vaccine started 6 days after serum	0	10	4	1	19
Vaccine	72	10	9	0	15
Serum	72	10	7	1	21
Serum, with vaccine started same day as serum	72	10	6	0	23
Serum, with vaccine started 3 days after serum	72	10	7	2	23
Serum, with vaccine started 7 days after serum	72	10	4	1	19
Controls		10	9	0	14
Do		10	7	0	19

[1] 0.25 cc. 1/10 whole emulsion dog brain street virus in masseter muscle.
[2] 1.5 percent formalized vaccine; 0.1 cc. subcutaneously daily for 21 days; vaccine potency at least 8,000 MLD.
[3] 1 dose of 1 cc. unconcentrated rabbit immune serum subcutaneously.

90 and 70 percent in the controls in the two parts of the experiment. It is apparent that serum alone administered either 3 or 72 hours after the introduction of the virus gave a slightly lower mortality than vaccine alone and a definitely longer average time to death. The interval between the administration of the serum and vaccine did not seem to make much difference when therapy was begun 3 hours after administration of virus, but when therapy was instituted 72 hours after virus the group with an interval of 7 days between serum and vaccine seemed superior from the standpoint of mortality although the average time to death was not increased.

MOUSE EXPERIMENTS (PROPHYLAXIS)

Groups of mice were inoculated into the gastrocnemius muscle with a 1/64 dilution of fixed virus. Due to variability of virulence this dilution in some experiments represented but one MLD and in others up to 13 MLD. The incubation period in control mice in these

experiments usually was about 7 days, the animals dying 4 to 5 days thereafter.

Table 7 shows an experiment in which serum alone locally was compared to serum with vaccine started 7 days later, when treatment was begun at 3, 24, 48, and 72 hours after virus. The virus dose of 1/64 dilution in this experiment represented 14 MLD. Both the mortality rates and the average days of survival are related to the interval from inoculation of virus to treatment in both groups. There are no real differences in mortality rates between serum alone and serum combined with vaccine but a definitely greater increase in survival time for the combined serum and vaccine treatment groups.

TABLE 7.—*Serum vs. serum and vaccine rabies prophylaxis in mice. Effect of interval from virus to treatment*

Treatment	Time from virus inoculation [1] to treatment (hours)	Total number of mice	Number developing rabies	Average time of survival (days)
Serum [2]	3	19	8	15.8
Do	24	24	19	13.3
Do	48	24	21	13.1
Do	72	25	24	12.2
Serum [2] and vaccine [3]	3	23	14	19.8
Do	24	25	20	15.8
Do	48	25	23	14.0
Do	72	25	23	12.6
Controls		22	22	12.0

[1] 0.03 cc. 1/64 dilution fixed virus in gastrocnemicus muscle—Virus titer 1/891.
[2] 1 dose of 0.05 cc. of 10 × concentrated rabbit immune serum locally at site of virus inoculation.
[3] 5-percent phenolized vaccine 0.05 cc. subcutaneously daily for 14 days starting 7 days after serum inoculation.

A more quantitative method of testing was used in the experiment shown in table 8. Serial dilutions of virus were given to mice and then groups immediately treated with concentrated normal rabbit serum locally, concentrated rabies immune rabbit serum locally, and concentrated immune serum intraperitoneally. Complete protection

TABLE 8.—*Rabies prophylaxis in mice by immune serum injected at site of vaccine inoculation vs. serum intraperitoneally*

Treatment [1]	Virus dilutions [2] (Rabies/total mice)									50 percent end point	MLD protection
	1/4	1/8	1/16	1/32	1/64	1/128	1/256	1/512	1/1024		
Normal serum [3] at site of virus inoculation	4/4	4/4	4/5	3/4	3/5	1/5	2/5	----	----	1/79	3
Immune serum [3] at site of virus inoculation	0/4	0/5	0/4	0/5	0/4	0/5	0/5	----	----	[4] 1/4	[5] 54
Immune serum [3] intraperitoneally	1/5	2/5	0/5	2/5	1/4	1/4	0/4	----	----	1/7	31
Controls	----	----	----	----	4/5	2/5	0/5	4/5	3/5	1/216	----

[1] 0.03 cc. dilution of fixed virus in gastrocnemicus muscle.
[2] All treatment given immediately after virus inoculation.
[3] Rabbit serum 10× concentrated, 1 dose of 0.05 cc.
[4] Less than.
[5] At least.

to all mice resulted when the immune serum was given at the site of virus inoculation and, although not complete, very good protection was obtained by immune serum given intraperitoneally.

In order to determine the relative immunity produced by the use of serum and vaccine alone and combined, the experiment shown in figure 1 was performed at varying time intervals during treatment. Groups of 150 mice each were started on treatment with serum, vaccine, serum with vaccine started the same day, and serum with vaccine started 6 days later. At 1, 6, and 11 days after the beginning of treatment groups of mice were given serial twofold dilutions of the

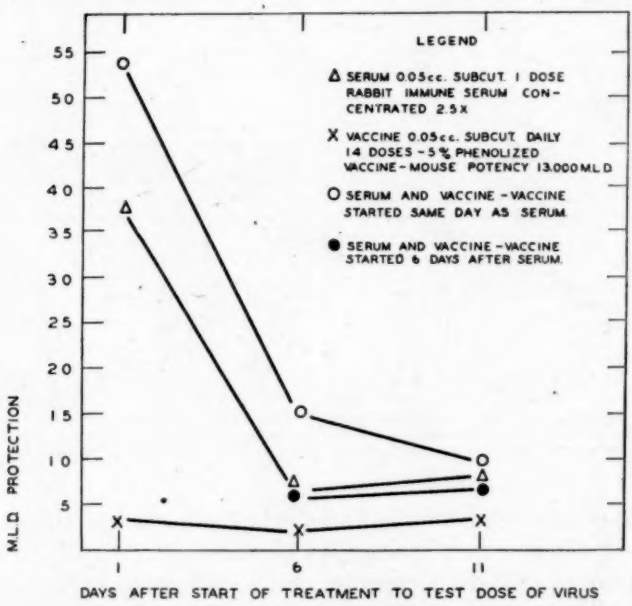

FIGURE 1.—Development of immunity in mice during administration of vaccine, immune serum alone, and combined with vaccine.

intramuscular strain of fixed virus in the gastrocnemius muscle. In those groups receiving vaccine the treatment was continued after the test virus had been given. The number of MLD protection was determined by the 50-percent end point method. Controls of the same age as the treated mice were run each time test virus was inoculated and the test virus was from one lot kept frozen at −70° C. Those mice receiving serum either alone or combined with vaccine had a high level of protection early with a dropping off as time elapsed from the day the serum had been given, but even 11 days later were still protected against more virus than the mice receiving vaccine alone. (See fig. 1.)

In the mouse experiment, the results of which are shown in table 9, serial dilutions of fixed virus from 1/4 to 1/256 dilutions were inoc-

TABLE 9.—*Serum alone and combined with vaccine vs. vaccine alone in postinfectious prophylaxis of rabies in mice*

Type of treatment	Protection by mouse protection test (50 percent end point)		
	Time interval from virus inoculation[1] to treatment		
	3 hours	24 hours	48 hours
Vaccine [2]	3 MLD	2	2
Serum [3]	17	6	13
Serum [3] and vaccine [2] started 6 days after serum	11	16	8

[1] 0.03 cc. of twofold dilutions of fixed virus into gastrocnemicus muscle; 7 mice inoculated with each dilution (1/4 to 1/256).
[2] 0.05 cc. of 5 percent phenolized vaccine subcutaneously daily for 10 days; vaccine potency 15,430 MLD.
[3] 0.05 cc. of concentrated rabbit immune serum, 1 dose, at site of virus inoculation.

ulated into the gastrocnemius muscle of 4-week-old Swiss mice, 0.03 cc. to a dose. Seven mice in each group were inoculated with each dilution. Mice were treated at 3, 24, and 48 hours after virus inoculation. The serum used had been concentrated but 5 times and only one dose of 0.05 cc. was given locally in the virus inoculation site. The vaccine was a 5-percent emulsion of phenolized virus whose potency by the mouse test was 15,430 MLD. It was administered in doses of 0.05 cc. subcutaneously daily for 10 doses. In the serum-and-vaccine-treated group the course of vaccine was started 6 days after the serum was given. In table 9, where the 50-percent end points of MLD's protection are tabulated, it is seen that serum, either alone or combined with vaccine, gave more protection than vaccine alone no matter at what interval treatment was started over the period tested (3 to 48 hours) and even at 48 hours after infection the serum therapy was effective.

MONKEY EXPERIMENT (PROPHYLAXIS)

In the monkey experiment summarized in table 10, three of the six controls died of rabies. However, no comparison could be made between vaccine and serum with vaccine, since no deaths occurred in

TABLE 10.—*Serum and vaccine, alone and combined, in rabies prophylaxis in monkeys*

Treatment [1]	Number of monkeys	Deaths	
		Rabies	Nonrabies
Vaccine [2]	6	0	0
Serum [3]	6	1	1
Serum [3] and vaccine [2] started 6 days after serum	6	0	0
Controls	6	3	1

[1] Treatment started 24 hours after 1.5 cc. 1/10 whole emulsion of first monkey passage brain street virus in each masseter muscle.
[2] 5 percent phenolized vaccine—2 cc. subcutaneously daily for 21 days; vaccine potency over 2,000 MLD.
[3] 1 dose of 10 cc. in thigh muscle of 10× concentrated rabbit immune serum.

these groups. One of six in the group receiving serum alone died of rabies. All monkeys in this experiment were tuberculin negative and were observed for 6 months. The two nonrabies deaths followed bleeding. All monkeys were bled before virus inoculation and at intervals of 5, 10, 15, 20, and 30 days thereafter. The serums of all monkeys drawn after a given interval in each treatment group were

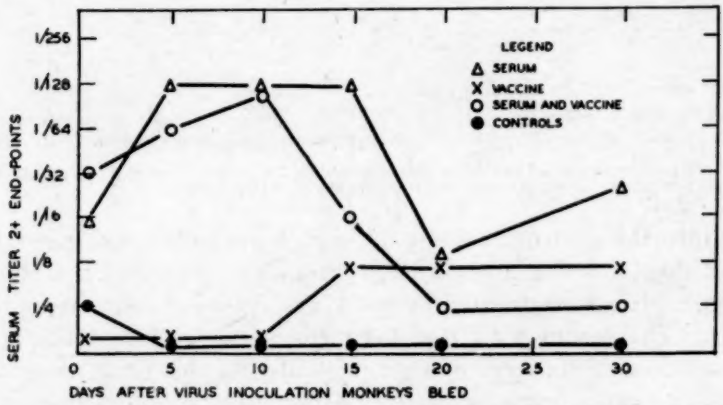

FIGURE 2.—Complement fixing antibody response in serum of monkeys after infection with street virus and during treatment with vaccine, with serum alone, and combined with vaccine.

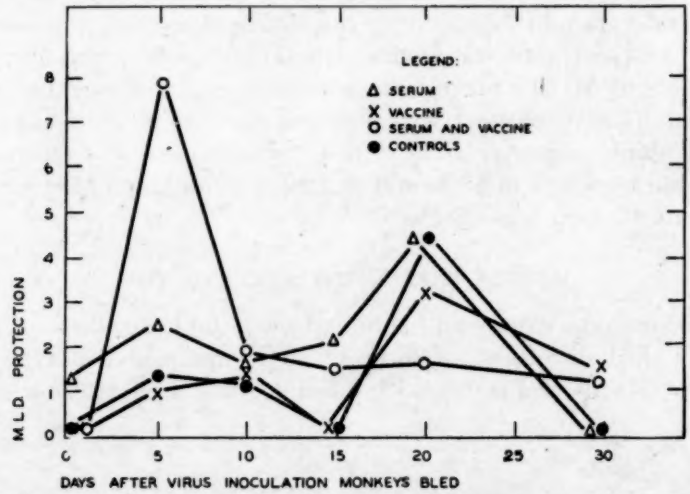

FIGURE 3.—Protective antibody response in serum of monkeys after infection with street virus and during treatment with vaccine, with serum alone, and combined with vaccine.

pooled and tested by complement fixation and the serum-protection mouse test. Figures 2 and 3 show the results. By both methods of testing the serum titers were high early in those groups receiving serum either alone or combined with vaccine. Later they tended to drop to an intermediate level, whereas the serums from monkeys receiving vaccine alone were at a low level early and rose to an inter-

mediate level later. It is interesting to see the relatively high level of protection developed in the serums of the control monkeys at the time they were actually coming down with rabies. These same control serums, however, never developed any complement-fixing antibodies.

DISCUSSION

At first glance the differences in mortality rates and the amount of protection afforded in the groups of animals receiving serum, alone or combined with vaccine, as compared to the controls, would not appear to be great. However, if one is familiar with the experimental results of investigations in rabies from Pasteur to the present, it becomes obvious that when the method of testing rabies prophylaxis corresponds to the method used in humans, namely, treatment begun at intervals after the peripheral introduction of virus, there have rarely been marked differences between control and vaccinated animals (*27*). Especially has this been true if treatment has been started at an interval of 24 hours or more after virus has been inoculated. A plausible explanation of this difference in results of vaccine prophylaxis in animals and in man would seem to be the usually much shorter incubation period in small animals. This is especially true in mice. In our experiments, using a fixed intramuscular strain of virus given peripherally, symptoms in the control mice appear as early as the seventh day. Webster (*28*) found that by using a highly potent vaccine (potency tested by preinfection immunization) the dose of fixed virus given intramuscularly had to be reduced to the point where only 50 percent of control mice died before he could show protection by postinfection immunization, giving the vaccine intraperitoneally. (Intraperitoneal immunization, of mice against rabies is always more effective than the same dose given subcutaneously.) Even this small degree of protection could not be demonstrated unless the vaccine was started within a few hours after virus inoculation.

Using this same type of technique, 0.05 cc. of concentrated immune serum has given us as high as 54 MLD protection if given immediately after virus inoculation and 13 MLD when given as long as 48 hours after infection.

The mechanism of infection and of prophylactic immunization in rabies has not as yet been completely explained. Experiments reported from this laboratory (*29*) have shown that street virus given intramuscularly remains viable locally up to 4 days but may invade the peripheral nerve and spinal cord as early as 2 days after injection. Subsequent spread centrally is slower. In immunized animals or those being immunized after infection, it was found that the virus remained viable locally in the muscle up to 4 days but its presence was not so consistent and it was not found in the nervous tissues.

Kligler and Bernkopf (*30*) have confirmed these results but state that once the virus has invaded the central nervous system in immunized animals its progression from there on is the same as in the controls. However, we have shown (*29*) and it has been confirmed by others (*31*) that the nervous tissue itself from an immunized animal after thorough washing has the ability to neutralize virus as compared to normal tissues. It would seem obvious that vaccine prophylaxis cannot produce immunity before the virus invades nervous tissue, a matter of 3 to 4 days at the most. However, the length of the incubation period of the disease probably depends on the time necessary for spread of virus within the central nervous system to those cells whose invasion results in symptoms and clinical disease. If that period is long enough, then immunity of the nervous tissue itself can be produced to prevent the virus from invading the vital cells.

Serum then could act in two ways, both probably extracellularly. First, the virus could be destroyed locally while still in the muscle. Secondly, the serum could retard the spread of virus within the nervous tissue once it is invaded, as evidenced in our experimental results where the incubation period was prolonged even though the animals were not completely protected. This prolongation of the incubation period is probably just what is needed for the vaccine to be effective, hence the better results in experiments using street virus when serum and vaccine were combined. As further evidence to support this explanation of the mechanism involved it should be pointed out that the limit of effectiveness of the serum, as far as preventing death in experimental animals is concerned, is about 3 days after virus inoculation. This also represents about the length of time that the virus remains viable locally.

These experimental results suggest that rabies serum prophylaxis in man would probably have several advantages. In the first place many of the "vaccine failures" have had a short incubation period (*32*), the failure probably being due to the fact that there is not sufficient time for the vaccine to produce immunity in the nervous tissue. The ability of the serum to prolong the incubation period in animals suggests that serum might make the vaccine effective in these cases. The use of serum locally at the site of the bite makes possible specific treatment while the virus is still localized. From the experimental results, serum alone would probably suffice in those patients having the type of exposure now requiring 14 doses of vaccine, whereas serum followed by a course of vaccine 6 days later would be indicated in those patients needing the 21-dose course of vaccine. It is well known that a large number of people receiving vaccine prophylaxis against rabies have not had a real exposure to the disease (*33*) and are thus being needlessly subjected to the discomfort and danger of 14 daily doses of vaccine. This is necessary because early treatment is indicated and

often the diagnosis in the biting animal is not at first definite. By present-day methods of rabies diagnosis in animals a definite answer is obtainable within 6 days after mouse inoculation (*34*). This interval of 6 days is also used in our combined serum and vaccine prophylaxis so that after a dose of serum at the time of a bite, a diagnosis of rabies could be established by mouse inoculation of the brain of the suspected animal in time to use the vaccine, and in case the mouse inoculation was negative, the patient would have received only 1 dose of serum.

SUMMARY

A method has been described for the production and concentration of rabies immune rabbit serum.

Serum prophylaxis alone as employed in these studies gave consistently better results than vaccine alone in the postinfection treatment of rabies in experimental animals.

Serum prophylaxis was apparent up to 3 days after infection, more effective when given intramuscularly at the site of virus inoculation than subcutaneously elsewhere on the body, and when used against street virus infection the results were better when combined with vaccine prophylaxis.

When combined with a course of vaccine treatment, serum prophylaxis probably is more effective if an interval of 6 days elapses between the dose of serum and the beginning of the vaccine course.

Experimental results warrant a trial of immune serum either alone or combined with vaccine in prophylaxis of rabies in man.

REFERENCES

(*1*) Babes, V., and Lepp: Researches of antirabies vaccination. Ann. de l'Inst. Pasteur, **3:** 385 (1889).

(*2*) Remlinger, P.: Contribution to the study of antirabies serum. Compt. Rend. Soc. de biol., **62:** 961 (1907).

(*3*) Babes, V., and Cerchez, Th.: Experiments on attenuation of fixed rabies virus. Ann. Inst. Pasteur, **5:** 625 (1891).

(*4*) Tizzoni, G., and Schwartz, R.: The prevention and cure of rabies by blood of vaccinated animals. Riforma, Naples, Med., Nos. 18 and 19 (1892).

(*5*) Ponomareff, A., and Tchechoff, A.: Conditions of action of antirabic serum in organism. Compt. Rend. Soc. de biol., **97:** 376 (1927).

(*6*) Loeffler, E., and Schweinburg, F.: Animal experiments with rabicidal serum. Wein. klin. Wchnschr, **45:** 813 (1932).

(*7*) Fermi, C.: Comparison of rabicidal and immunizing power of antibodies serum of different animals and of different institutes. Centralblat. f. Bakt., **52:** 576 (1909).

(*8*) Fermi, C.: Wirking der antiwutimpfstoffe und sera je nach der tierspecies, aus Welcher sie ent stammen und welcher sie verabreicht werden. Centralblat. f. Bakt., **49:** 452 (1909).

(*9*) Kraus, R., and Holobut, T.: Ueber die Wirkung des intrackulin injezierten rabiziden serums. Ztschr. f. Immunitatsforsch u. exper. Therap., **3:** 130 (1909).

(*10*) Marie, A.: Researches on antirabies serum. Ann. Inst. Pasteur, **22:** 271 (1908).

(*11*) Proca, G., Babes, S., and Jonnesco, D.: Preventive serotherapy in rabies—experimental study with guinea pigs. Compt. Rend. Soc. de biol., **115:** 1001 (1934).

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(12) Proca., G., Babes, S., and Jonnesco, D.: Intracaudal inoculation of rabies virus and serotherapy of rabies. Compt. Rend. Soc. de biol., **115:** 1313 (1934).
(13) Proca, G., Babes, S., and Jonnesco, D.: Some attempts at local serotherapy of rabies. Compt. Rend. Soc. de biol., **117:** 133 (1934).
(14) Proca, G., Babes, S., and Jonnesco, D.: Serotherapy of rabies. Bull. Acad. Med. Roumanie, **4:** 609 (1937).
(15) Jonnesco, D.: Researches on an antirabies serum. Compt. Rend. Soc. de biol., **130:** 1145 (1939).
(16) Shortt, H. E., McGuire J. P., Brooks, A. G., and Stephens, E. D.: Rabies immunization: probable lines of progress in improvement of methods. Ind. J. Med. Res., **22:** 537 (1935).
(17) Covell, G., McGuire, J. P., Stephens, E. D., and Lahiri, B. N.: Rabies immunization. Ind. J. Med. Res., **24:** 373 (1936).
(18) Smith, R. O. A.: Rabies immune serum and vaccine therapy in humans. Rep. Sci. Adm. Bd. Ind. Res. Fund. Assoc., p. 64, 1937.
(19) Hoyt, A., Fisk, R., and Moore, F. J.: Experimental rabies in white mice. Studies on passive immunity, I. Proc. Soc. Exp. Biol. & Med., **32:** 1560 (1935).
(20) Hoyt, A., Fish, R. T., Moore, F. J., and Tracy, R. L.: Experimental rabies in white mice. Studies on passive immunity, II. J. Inf. Dis., **59:** 152 (1936).
(21) Hoyt, A., and Gurley, M. K.: Experimental street virus rabies in white mice. Proc. Soc. Exp. Biol. & Med., **37:** 454 (1937); **38:** 40 (1938).
(22) Hoyt, A., Moore, F. J., Gurley, M. L., and Warner, D.: Experiments on antirabic immunization. J. Bact., **36:** 287 (1938).
(23) Yen, C. H.: Protective value of antiviral serum in experimental rabies infection. Proc. Soc. Exp. Biol. & Med., **49:** 533 (1942).
(24) Casals, J., and Palacios, R.: The complement fixation test in the diagnosis of virus infections of the central nervous system. J. Exp. Med., **74:** 409 (1941).
(25) Felton, L. D.: Concentration of pneumococcus antibody. J. Inf. Dis., **43:** 543 (1928).
(26) Habel, K.: Evaluation of a mouse test for the standardization of the immunizing power of antirabies vaccines. Pub. Health Rep., **55:** 1473 (1940).
(27) Webster, L. T.: The immunizing potency of antirabies vaccines. A critical review. Am. J. Hyg., **30:** 113 (1939).
(28) Webster, L. T., and Casals, J: An improved non-virulent rabies vaccine. Am. J. Pub. Health, **32:** 268 (1942).
(29) Habel, K.: Tissue factors in antirabies immunity of experimental animals. Pub. Health Rep., **56:** 692 (1941).
(30) Kligler, I. J., and Bernkopf, H.: The path of dissemination of rabies virus in the body of normal and immunized mice. Brit. J. Exp. Path., **24:** 15 (1943).
(31) Kubes, V., and Gallia, F.: Brain tissue neutralization, a new biological reaction for rabies virus. Bol. Del. Inst. de Invest. Vet., **1:** 105 (1943).
(32) Blatt, M. L., Hoffman, S. J., and Schneider, M.: Report of twelve cases of rabies with discussion of prophylaxis. J. Am. Med. Assoc., **111:** 688 (1938).
(33) Denison, G. A., McAlpine, J. G., and Gill, D. G.: Rabies deaths in Alabama and analysis of case histories concerning treatment. Am. J. Pub. Health, **27:** 869 (1937).
(34) Leach, C. N.: Comparative methods of diagnosis of rabies in animals. Am. J. Pub. Health, **28:** 162 (1938).

TESTS OF EPIDEMIC TYPHUS VACCINES[1]

By RICHARD DONOVICK and RALPH W. G. WYCKOFF

Large-scale production of vaccine against epidemic typhus fever was begun in this country about two years ago mainly as the result of Cox's demonstration that the causative rickettsiae of this disease

[1] From the Lederle Laboratories, Inc., Pearl River, N. Y. This paper was approved for publication September 11, 1942, and scheduled for publication in PUBLIC HEALTH REPORTS in the issue of October 16, 1942. Because of the subject matter the paper was withheld from publication at that time.

multiply readily in the yolk membrane of developing chicken embryos (*1*). Since that time steady improvement has been made in the quality of such vaccines, both in the direction of increasing the total infectiousness of the material from which they are prepared and in the methods available for the subsequent detoxification and refinement of this material. Methods of estimating vaccine potency have changed to measure this development.

The most direct laboratory method of testing epidemic typhus vaccine is one in which the immunity of vaccinated guinea pigs is challenged by injecting enough infectious tissue to produce typical guinea pig typhus in control animals. This test is hard to use routinely because it requires several weeks to carry out and because it is very easily invalidated by intercurrent infections since a characteristic febrile response extending over several days is the only clear-cut clinical evidence of epidemic typhus infection in guinea pigs. Bengtson and Topping's development of the complement fixation test for typhus (*2, 3, 4*) gives one of several other (*5*) feasible ways for evaluating typhus vaccine. During the past months we have been comparing the complement fixing antibody titres and results of protection tests on guinea pigs injected with many different typhus vaccines. It has been our experience that results of these two tests run parallel in the sense that vaccines which show an especially high degree of protective power also induce a particularly high average complement fixing antibody titre.

This is readily illustrated by table 1 which contains representative data comparing three different vaccines. These vaccines, prepared from a common pool of inactivated yolk membrane, varied in the method used for their refinement. Each corresponds to an initial tissue content of 8 percent. The vaccine designated IA was refined by a development of the phenol method described by Cox (*6*); a similar procedure was followed in preparing vaccine IIA except that another chemical was used in place of phenol; vaccine IIIA was processed along lines suggested by Dr. N. H. Topping of the National Institute of Health, United States Public Health Service.

It is evident from both the temperature charts and the serum-complement fixation end points that vaccine IIIA is superior to the other two. This has been confirmed by repeated experiments with these vaccines and with duplicate preparations similarly refined. It is hoped that the results of these experiments can be published more fully in the future.

Tests such as the foregoing measure the improvement effected in epidemic typhus vaccines over the last year. It is improbable that any vaccine made a year or more ago would have shown either a demonstrable protection or a complement fixing antibody titre exceeding 1/2 when tested under the conditions reported in table 1.

TABLE 1.—*The complement fixation titres of vaccinated guinea pigs and the temperatures of typical animals after challenge injections*

Animal number	Vaccine dose (cc.)	Vaccine	Temperatures (degrees C.) on X days following challenge injections										Average complement fixation end point dilution
			6	7	8	9	10	11	12	13	14	15	
954	0.1	IA	39.4	39.1	*40.6*	39.6	*40.0*	*39.7*	*39.8*	*40.5*	*39.7*	39.5	1/2
955	.1	IA	39.1	39.5	39.3	*39.7*	*40.0*	*39.9*	39.6	39.5	39.4	39.1	
956	.1	IA	39.1	39.5	39.5	*39.7*	*39.9*	*39.8*	*40.2*	*40.1*	*40.0*	*39.9*	
972	.1	IIA	39.0	39.0	39.5	39.1	38.9	39.0	39.5	39.4	39.0	39.2	1/16
973	.1	IIA	39.2	38.7	38.9	38.8	38.7	38.6	38.4	38.8	38.5	39.5	
974	.1	IIA	39.1	39.4	39.6	*40.0*	*39.9*	*40.0*	*39.8*	*40.0*	39.5	*40.0*	
991	.1	IIIA	39.0	39.0	38.9	38.7	38.7	38.9	38.8	38.9	38.4	38.2	1/64
992	.1	IIIA	38.9	38.9	39.0	38.6	39.0	38.6	38.9	38.9	38.8	38.9	
948	.25	IA	38.9	38.7	38.9	38.9	38.8	39.0	38.7	38.8	38.7	38.7	1/32
950	.25	IA	39.5	*39.8*	39.5	*39.9*	*39.8*	*39.8*	*40.0*	*39.9*	39.6	*40.0*	
966	.25	IIA	39.1	39.4	38.2	39.5	39.5	39.6	*39.8*	*39.7*	39.5	39.5	1/32
967	.25	IIA	39.0	38.7	38.9	38.8	39.2	38.9	39.4	*39.7*	*39.7*	39.4	
968	.25	IIA	38.9	39.0	39.1	39.5	39.2	39.0	39.4	39.3	39.1	39.2	
984	.25	IIIA	39.1	39.2	39.1	39.4	39.2	38.9	39.4	39.0	39.0	38.8	1/128
985	.25	IIIA	38.4	38.7	38.8	38.4	38.9	39.1	39.1	38.9	38.6	38.8	
749	0	----------	39.5	39.5	*40.6*	*40.1*	*40.1*	*40.5*	*40.4*	*40.5*	39.5	*39.8*	----------
750	0	----------	39.4	*40.0*	*39.9*	*40.1*	*40.6*	*40.6*	*40.7*	*40.4*	39.4	38.7	----------
751	0	----------	39.4	39.5	39.5	*40.0*	*40.0*	*40.1*	*40.4*	*40.2*	*39.8*	39.5	----------
752	0	----------	*39.7*	*40.0*	*40.0*	*40.6*	*40.0*	*40.5*	*40.2*	*40.0*	39.6	38.9	----------

NOTE.—The challenge injection consisted of 1 cc. (introduced intraperitoneally) of a freshly prepared 10 percent suspension of the brain of a Breinl typhus-infected guinea pig killed on the third day of fever. Temperatures of 39.7° C. and higher are taken as evidence of a febrile reaction. They are indicated by italics.

The serums used in the complement fixation reactions were obtained from heart bleedings made 10 days after the first (3 days after the second) vaccination. The complement fixation end point dilutions in the table are averages from the serums of more vaccinated guinea pigs than those listed in the table.

Only the best lots then gave complete protection against a challenge inoculum of 1 cc. of a 10 percent suspension of infectious brain when the vaccine dose was 1 cc. (as contrasted with the 0.1-cc. and the 0.25-cc. doses of table 1). The serum-complement fixation titres of table 1 apply to bleedings made 10 days after the first vaccination; such titres are higher after a longer time interval as well as after larger doses of vaccine. Thus the average titre from guinea pigs bled 2 weeks after two 1-cc. vaccinations with vaccine IIIA was 1/512. Our experience indicates that such vaccination with products made a year ago would rarely, if ever, have resulted in serums with titres in excess of 1/16.

Though data such as these make it clear that present typhus vaccines are definitely superior to those prepared a year ago, there is no reason to assume that a limit has yet been reached to this improvement.

REFERENCES

(*1*) Cox, H. R.: Use of yolk sac of developing chick embryo as medium for growing rickettsiae of Rocky Mountain spotted fever and typhus groups. Pub. Health Rep., **53**: 2241 (1938).

(*2*) Bengtson, Ida A.: Complement fixation in endemic typhus fever. Pub. Health Rep., **56**: 649 (1941).

(3) Bengtson, Ida A., and Topping, Norman H.: The specificity of the complement fixation test in endemic typhus fever using a rickettsial antigen. Pub. Health Rep., 56: 1723 (1941).
(4) Bengtson, I. A., and Topping, N. H.: Complement-fixation in rickettsial diseases. Am. J. Pub. Health, 32: 48 (1942).
(5) Snyder J. C., and Anderson, C. R.: Susceptibility of eastern cotton rat, *Sigmodon hispidus hispidus*, to European typhus. Science, 95: 23 (1942).
(6) Cox, H. R.: Cultivation of rickettsiae of Rocky Mountain spotted fever, typhus, and Q fever groups in embryonic tissues of developing chicks. Science, 94: 399 (1941).

PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES

March 25–April 21, 1945

The accompanying table summarizes the prevalence of nine important communicable diseases, based on weekly telegraphic reports from State health departments. The reports from each State for each week are published in the Public Health Reports under the section "Prevalence of disease." The table gives the number of cases of these diseases for the 4 weeks ended April 21, 1945, the number reported for the corresponding period in 1944, and the median number for the years 1940–44.

DISEASES ABOVE MEDIAN PREVALENCE

Diphtheria.—For the 4 weeks ended April 21 there were 1,008 cases of diphtheria reported as compared with 781 during the corresponding period in 1944, and a 5-year (1940–44) median of 903 cases. The New England, East North Central, West South Central, and Pacific sections reported excesses over the preceding 5-year median; in the East South Central section the incidence was about normal, and in the other four geographic regions the numbers of cases fell below the normal seasonal expectancy. For the country as a whole the current incidence is the highest reported during the corresponding weeks in 5 years. Of a total of 82 cases reported from Michigan for the current 4 weeks, 44 occurred in Oakland County during the week ended March 31.

Meningococcus meningitis.—A total of 794 cases of this disease was reported during the current 4-week period. With the exception of the epidemic years of 1943 and 1944 the incidence was the highest recorded for this period since 1936. Of the total cases, New York reported 89, California 81, Illinois 64, Pennsylvania and Texas 47 each, Tennessee 26, Maryland 25, Michigan 24, Massachusetts and Missouri 23 each, and Virginia 22 cases; almost two-thirds of the cases occurred in those 11 States. For the entire reporting area the number of cases was only about 40 percent of the 1944 incidence, but it was more than twice the 1940–44 median for this period. The

incidence in each geographic section was considerably below that of 1944, but the New England section alone reported fewer cases than the median expectancy.

Poliomyelitis.—The current 4-week total of 128 cases of poliomyelitis was the highest number reported for the corresponding period in the 17 years for which these data are available. Of the total cases, New York reported 25, Texas and Alabama 19 each, Michigan and California 6 each, but no other State reported more than 4 cases. For the country as a whole the number of reported cases was about 50 percent above the 1940–44 median level. By geographic regions the disease was relatively high in the Middle Atlantic, East North Central, East South Central, and West South Central regions; about normal in the New England, West North Central, and South

Number of reported cases of 9 communicable diseases in the United States during the 4-week period March 25–April 21, 1945, the number for the corresponding period in 1944, and the median number of cases reported for the corresponding period, 1940–44

Division	Current period	1944	5-year median	Current period	1944	5-year median	Current period	1944	5-year median
	Diphtheria			Influenza [1]			Measles [2]		
United States	1,008	781	903	7,352	8,650	12,335	16,857	126,484	104,809
New England	32	29	24	147	108	27	1,100	8,710	8,710
Midde Atlantic	129	99	155	30	72	72	1,647	20,955	20,955
East North Central	166	99	142	180	427	510	1,528	26,395	26,395
West North Central	70	60	82	46	189	189	686	10,424	8,226
South Atlantic	131	114	141	1,825	2,486	4,171	1,368	22,005	11,745
East South Central	85	68	83	278	606	1,076	407	3,443	3,443
West South Central	169	136	152	4,277	3,809	4,543	2,730	15,895	8,672
Mountain	50	29	66	450	609	681	1,192	4,643	4,643
Pacific	176	147	84	119	344	511	6,199	14,014	7,945
	Meningococcus meningitis			Poliomyelitis			Scarlet fever		
United States	794	2,012	389	128	80	74	20,892	29,089	17,096
New England	39	130	45	2	1	2	2,211	2,499	1,876
Middle Atlantic	155	440	132	30	10	5	5,679	6,540	5,470
East North Central	152	460	25	15	7	7	5,160	7,992	5,632
West North Central	72	152	16	5	4	5	1,705	3,385	1,552
South Atlantic	122	259	76	14	9	10	1,958	2,836	897
East South Central	68	175	41	30	5	6	509	782	782
West South Central	73	145	27	24	20	10	617	585	374
Mountain	10	82	5	1	3	5	907	1,309	494
Pacific	103	169	28	7	21	12	2,146	3,161	778
	Smallpox			Typhoid and paratyphoid fever			Whooping cough [2]		
United States	54	37	105	230	255	299	10,035	6,805	14,201
New England	0	0	0	7	7	14	1,124	527	1,217
Middle Atlantic	0	0	0	37	40	47	1,997	960	3,164
East North Central	21	5	37	26	27	36	1,468	848	2,902
West North Central	12	8	21	5	8	10	243	362	531
South Atlantic	2	3	6	59	63	63	1,610	1,533	1,942
East South Central	3	4	6	25	19	23	297	463	666
West South Central	5	8	32	52	39	50	1,160	946	1,399
Mountain	5	8	2	13	15	15	474	547	815
Pacific	6	1	6	6	37	20	1,662	619	1,722

[1] Mississippi and New York excluded; New York City included.
[2] Mississippi excluded.

Atlantic sections; and below normal in the Mountain and Pacific sections.

Scarlet fever.—For the country as a whole the incidence of scarlet fever (20,892 cases) was about 70 percent of the number of cases reported during the same weeks in 1944. The 1940–44 median for the corresponding period was approximately 17,000 cases. The number of cases was lower than in 1944 in all sections of the country except the West South Central. Compared with the 1940–44 median the disease was more prevalent than might be expected in all geographic regions except the East North Central and East South Central sections.

DISEASES BELOW MEDIAN PREVALENCE

Influenza.—The incidence of this disease was relatively low, the number of cases reported (7,352) being about 85 percent of the 1944 figure for these same weeks, and 60 percent of the preceding 5-year median. The number of cases (147) in the New England section was almost five times the median expectancy, but in each of the other geographic regions the number of cases was lower than the normal seasonal incidence.

Measles.—For the country as a whole the number of cases (16,857) of measles reported for the current 4-week period was the lowest recorded for this period in the 17 years for which these data are available. In 1944 there were 126,484 cases reported for the corresponding 4 weeks and the 1940–44 median was approximately 105,000 cases. The situation was favorable in all sections of the country, each geographic region reporting a decline from the preceding year's figures, as well as from the preceding 5-year median figures.

Smallpox.—For the current 4-week period there were 54 cases of smallpox reported. The number represented a 50-percent decrease from the 1940–44 median. Increases over the 1944 incidence were reported from the East North Central, West North Central, and Pacific regions, but the Mountain section alone reported an excess over the 1940–44 median.

Typhoid and paratyphoid fever.—Typhoid fever continued at a favorably low level. For the 4 weeks ended April 21 there were 230 cases reported as compared with 255 in 1944 and a median of 299 cases for the corresponding period in the preceding 5 years. In the South Atlantic, East and West South Central, and Mountain sections the incidence was about normal, while the New England, Middle Atlantic, East and West North Central, and Pacific sections reported very significant decreases from the seasonal median expectancy.

Whooping cough.—The number of cases (10,035) of this disease reported for the current 4-week period was 1.5 times the 1944 figure

for the corresponding 4 weeks, but it was only about 70 percent of the preceding 5-year median figure. All geographic regions were high in relation to 1944 except the West North Central, East South Central, and Mountain sections, but all sections were low in comparison with the 1940–44 medians.

MORTALITY, ALL CAUSES

For the 4 weeks ended April 21 there were 36,515 deaths from all causes reported by 93 large cities to the Bureau of the Census. The preceding 3-year (1942–44) average was 37,147 deaths. The deaths for each of the first 3 weeks of the period under consideration were lower than the 3-year average, but during the fourth week the number was about 0.7 percent above the average.

INCIDENCE OF HOSPITALIZATION, MARCH 1945

Through the cooperation of the Hospital Service Plan Commission of the American Hospital Association, data on hospital admissions among members of Blue Cross Hospital Service Plans are presented monthly. These plans provide prepaid hospital service. The data cover hospital service plans scattered throughout the country, mostly in large cities.

Item	March	
	1944	1945
1. Number of plans supplying data	68	82
2. Number of persons eligible for hospital care	11,605,270	17,046,176
3. Number of persons admitted for hospital care	98,151	144,576
4. Incidence per 1,000 persons, annual rate, during current month (daily rate × 365)	99.5	99.8
5. Incidence per 1,000 persons, annual rate for the 12 months ended March 31	104.6	103.6
6. Number of plans reporting on hospital days	24	25
7. Days of hospital care per case discharged during month [1]	8.61	8.32

[1] Days include entire stay of patient in hospital whether at full pay or at a discount.

DEATHS DURING WEEK ENDED APRIL 21, 1945

[From the Weekly Mortality Index, issued by the Bureau of the Census, Department of Commerce]

	Week ended Apr. 21, 1945	Corresponding week, 1944
Data for 92 large cities of the United States:		
Total deaths	9,032	9,216
Average for 3 prior years	8,973	
Total deaths, first 16 weeks of year	152,317	159,052
Deaths under 1 year of age	628	605
Average for 3 prior years	602	
Deaths under 1 year of age, first 16 weeks of year	10,097	10,030
Data from industrial insurance companies:		
Policies in force	67,216,667	66,380,649
Number of death claims	14,379	13,160
Death claims per 1,000 policies in force, annual rate	11.2	10.4
Death claims per 1,000 policies, first 16 weeks of year, annual rate	11.0	11.2

PREVALENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

REPORTS FROM STATES FOR WEEK ENDED APRIL 28, 1945

Summary

A total of 28 cases of poliomyelitis was reported for the current week, as compared with 32 last week, 18 for the corresponding week last year, and a 5-year (1940–44) median of 17. States reporting the largest numbers (last week's figures in parentheses) are as follows: New York 6 (6), Florida 5 (2), Texas 6 (11), California 4 (2). The total for the first 17 weeks of the year is 581, as compared with 375 for the same period last year and a 5-year median of 401.

Of the total of 202 cases of meningococcus meningitis, as compared with 190 last week, 94 occurred in 7 States, as follows (last week's figures in parentheses): New York 19 (32), Pennsylvania 13 (11), Ohio 9 (6), Illinois 11 (11), Florida 11 (5), Texas 15 (9), California 16 (28). The cumulative total of 4,009 cases for the first 17 weeks of the year is only 46 percent of the average for the same periods of the past 2 years, but more than 3 times the 5-year median for the period (1,311 cases), and, except the past 2 years, is more than reported for the corresponding period of any other year since 1936.

Figures for the first 17 weeks of the year for certain other diseases (last year's corresponding figures in parentheses) are as follows: Diphtheria 4,927 (3,994), dysentery (all forms) 9,921 (5,247), infectious encephalitis 114 (188), influenza 57,670 (328,181), measles 49,965 (428,804), Rocky Mountain spotted fever 16 (12), scarlet fever 93,885 (105,615), smallpox 175 (198), tularemia 285 (172), typhoid and paratyphoid fever 996 (1,223), endemic (murine) typhus fever 822 (650), whooping cough 42,080 (30,707).

A total of 9,103 deaths was recorded during the week in 93 large cities of the United States, as compared with 9,109 last week, 9,322 for the corresponding week last year, and a 3-year (1942–44) average of 9,375. The cumulative figure is 162,730, as compared with 169,762 for the same period last year.

Telegraphic morbidity reports from State health officers for the week ended April 28, 1945, and comparison with corresponding week of 1944, and 5-year median

In these tables a zero indicates a definite report, while leaders imply that, although none was reported, cases may have occurred.

Division and State	Diphtheria			Influenza			Measles			Meningitis, meningococcus		
	Week ended—		Median 1940–44	Week ended—		Median 1940–44	Week ended—		Median 1940–44	Week ended—		Median 1940–44
	Apr. 28, 1945	Apr. 29, 1944		Apr. 28, 1945	Apr. 29, 1944		Apr. 28, 1945	Apr. 29, 1944		Apr. 28, 1945	Apr. 29, 1944	
NEW ENGLAND												
Maine	0	0	0	-----	15	1	1	441	148	2	4	3
New Hampshire	0	3	0	1	3	-----	60	35	35	1	0	0
Vermont	0	0	0	-----	-----	-----	11	109	109	0	0	0
Massachusetts	5	2	3	-----	-----	-----	215	1,017	1,190	6	12	5
Rhode Island	1	1	1	33	-----	-----	0	98	98	1	1	1
Connecticut	2	0	0	3	-----	-----	128	527	447	2	6	2
MIDDLE ATLANTIC												
New York	14	9	20	[1] 2	[1] 3	[1] 8	62	1,836	1,836	19	56	18
New Jersey	1	5	5	5	2	10	46	1,505	1,505	6	21	3
Pennsylvania	3	9	11	1	2	-----	343	956	1,297	13	34	12
EAST NORTH CENTRAL												
Ohio	4	4	7	3	19	19	47	698	568	9	41	1
Indiana	3	5	5	1	5	8	54	198	198	4	12	0
Illinois	4	6	19	1	7	9	141	918	918	11	43	3
Michigan [2]	5	8	2	1	5	5	169	1,078	1,078	7	23	0
Wisconsin	2	4	1	54	61	52	70	2,816	1,703	3	9	2
WEST NORTH CENTRAL												
Minnesota	4	3	3	-----	-----	1	10	804	322	1	1	0
Iowa	2	2	2	-----	10	1	59	212	273	4	6	0
Missouri	1	0	1	3	1	3	20	308	308	7	22	2
North Dakota	0	1	1	-----	1	7	15	70	45	0	0	0
South Dakota	3	1	0	-----	-----	-----	16	30	20	0	0	0
Nebraska	4	0	1	3	3	3	92	255	255	1	2	0
Kansas	2	1	3	-----	7	7	64	723	630	4	9	1
SOUTH ATLANTIC												
Delaware	0	0	0	-----	-----	-----	4	15	15	0	2	1
Maryland [2]	14	20	4	3	4	8	25	609	409	4	6	6
District of Columbia	0	0	0	-----	2	-----	8	229	132	2	4	4
Virginia	11	2	5	70	108	175	66	613	381	7	10	10
West Virginia	3	2	2	2	13	14	45	446	133	2	4	3
North Carolina	5	6	5	-----	1	12	33	1,701	686	4	5	2
South Carolina	8	6	4	258	267	291	53	371	150	2	4	1
Georgia	4	3	3	8	5	29	22	79	211	1	10	1
Florida	6	7	3	1	14	14	28	289	289	11	2	1
EAST SOUTH CENTRAL												
Kentucky	4	3	4	-----	3	5	28	169	169	5	12	2
Tennessee	3	3	3	30	28	51	70	232	232	6	14	4
Alabama	14	9	7	13	45	65	19	323	263	8	6	4
Mississippi [2]	4	5	5	-----	-----	-----	-----	-----	-----	3	5	2
WEST SOUTH CENTRAL												
Arkansas	3	3	4	40	52	52	61	241	152	4	2	1
Louisiana	5	2	5	22	4	[1] 3	57	102	67	0	8	1
Oklahoma	3	5	2	17	90	76	33	382	184	1	2	2
Texas	29	29	24	654	711	711	654	4,182	1,541	15	18	4
MOUNTAIN												
Montana	1	0	2	15	12	12	14	115	115	1	1	0
Idaho	0	0	0	1	-----	-----	52	33	33	2	0	0
Wyoming	0	0	0	-----	-----	1	14	67	67	0	1	0
Colorado	3	13	11	11	22	22	15	246	308	2	2	0
New Mexico	2	2	1	6	7	1	13	111	72	1	0	0
Arizona	0	3	0	85	58	88	27	322	110	0	0	0
Utah [2]	0	0	0	11	-----	5	270	44	154	0	0	0
Nevada	0	0	0	217	100	-----	2	19	1	0	1	0
PACIFIC												
Washington	2	1	1	-----	-----	-----	241	256	318	3	5	2
Oregon	0	3	4	9	20	17	76	163	362	1	1	1
California	22	23	15	10	24	80	1,360	4,002	854	16	22	3
Total	206	211	211	1,594	1,734	1,741	4,913	29,995	26,526	202	449	80
17 weeks	4,927	3,994	4,826	57,670	328,181	159,244	49,965	428,804	314,834	4,009	9,083	1,311

[1] New York City only.

[2] Period ended earlier than Saturday.

Telegraphic morbidity reports from State health officers for the week ended April 28, 1945, and comparison with corresponding week of 1944, and 5-year median—Con.

Division and State	Poliomyelitis			Scarlet fever			Smallpox			Typhoid and paratyphoid fever [3]		
	Week ended—		Median 1940–44	Week ended—		Median 1940–44	Week ended—		Median 1940–44	Week ended—		Median 1940–44
	Apr. 28, 1945	Apr. 29, 1944		Apr. 28, 1945	Apr. 29, 1944		Apr. 28, 1945	Apr. 29, 1944		Apr. 28, 1945	Apr. 29, 1944	
NEW ENGLAND												
Maine	0	0	0	48	73	18	0	0	0	0	2	0
New Hampshire	0	0	0	5	20	7	0	0	0	0	0	0
Vermont	0	0	0	20	10	10	0	0	0	0	1	1
Massachusetts	0	1	0	315	426	326	0	0	0	5	2	2
Rhode Island	0	0	0	27	11	11	0	0	0	0	1	0
Connecticut	0	1	0	83	102	102	0	0	0	0	1	1
MIDDLE ATLANTIC												
New York	6	0	0	580	577	577	0	0	0	5	3	7
New Jersey	0	0	0	140	359	267	0	0	0	0	3	0
Pennsylvania	0	0	1	502	844	476	0	0	0	6	1	3
EAST NORTH CENTRAL												
Ohio	1	0	0	397	588	317	0	0	0	4	1	1
Indiana	0	0	0	95	131	127	0	2	2	1	2	1
Illinois	0	1	0	277	495	313	0	0	1	0	1	1
Michigan [2]	1	0	0	251	404	250	1	1	0	1	2	2
Wisconsin	0	1	0	178	394	171	0	0	1	1	1	0
WEST NORTH CENTRAL												
Minnesota	1	0	0	91	172	72	0	0	0	1	0	0
Iowa	0	0	0	59	117	50	0	0	1	0	1	1
Missouri	0	0	0	82	170	87	0	0	1	0	3	1
North Dakota	1	0	0	35	49	9	0	0	0	0	0	0
South Dakota	0	0	0	17	16	16	0	2	0	0	0	0
Nebraska	0	1	0	113	125	19	0	0	0	0	0	0
Kansas	0	1	0	106	122	75	0	0	0	0	1	1
SOUTH ATLANTIC												
Delaware	0	0	0	7	18	18	0	0	0	0	0	0
Maryland [2]	0	0	0	146	222	96	0	0	0	0	2	2
District of Columbia	0	0	0	23	145	20	0	0	0	0	0	0
Virginia	0	1	1	81	64	33	0	0	0	0	5	3
West Virginia	0	0	0	68	93	44	0	0	0	1	1	2
North Carolina	0	0	0	51	37	26	0	0	0	3	2	2
South Carolina	0	0	0	13	2	2	0	0	0	2	1	1
Georgia	0	0	0	20	43	15	0	0	0	5	8	3
Florida	5	0	0	16	9	7	0	0	0	6	2	2
EAST SOUTH CENTRAL												
Kentucky	0	0	0	71	83	83	0	1	0	10	0	2
Tennessee	1	1	0	45	96	65	0	0	0	3	3	2
Alabama	0	0	1	25	19	13	0	0	1	0	3	1
Mississippi [2]	0	1	1	7	2	7	0	0	0	4	1	1
WEST SOUTH CENTRAL												
Arkansas	0	0	0	6	11	7	0	0	1	0	3	1
Louisiana	0	4	0	15	12	5	1	1	1	7	3	6
Oklahoma	0	0	0	12	22	12	0	0	0	2	2	0
Texas	6	2	2	100	225	43	0	1	3	17	4	6
MOUNTAIN												
Montana	0	0	0	22	39	29	0	0	0	1	0	0
Idaho	0	0	0	37	54	11	0	0	0	2	0	0
Wyoming	0	0	0	5	13	12	0	0	0	0	0	0
Colorado	0	0	0	45	44	44	0	0	0	0	2	1
New Mexico	0	0	0	12	18	7	0	0	0	1	0	0
Arizona	0	0	0	55	27	6	0	0	0	1	0	0
Utah [2]	0	0	0	23	79	13	0	0	0	0	0	0
Nevada	0	0	0	0	3	0	1	0	0	0	0	0
PACIFIC												
Washington	2	0	0	115	334	41	0	1	0	0	0	0
Oregon	0	0	0	32	153	13	0	0	0	0	0	1
California	4	3	3	426	367	133	0	0	0	3	9	5
Total	28	18	17	4,899	7,439	4,104	3	9	35	92	77	87
17 weeks	581	375	401	93,885	105,615	67,902	175	198	459	996	1,223	1,284

[2] Period ending earlier than Saturday.

[3] Including paratyphoid fever reported separately, as follows: Massachusetts 4; New York 2; Georgia 1; California 1.

Telegraphic morbidity reports from State health officers for the week ended Apr. 28, 1945, and comparison with corresponding week of 1944, and 5-year median—Con.

Division and State	Whooping cough			Week ended Apr. 28, 1945							
	Week ended—			Dysentery			Encephalitis, infectious	Rocky Mt. spotted fever	Tularemia	Typhus fever	Undulant fever
	Apr. 28, 1945	Apr. 29, 1944	Median 1940–44	Amebic	Bacillary	Unspecified					
NEW ENGLAND											
Maine	32	18	18	0	0	0	0	0	1	0	0
New Hampshire	0	3	2	0	0	0	0	0	0	0	0
Vermont	25	13	14	0	0	0	0	0	0	0	0
Massachusetts	129	96	150	0	0	0	0	0	0	0	0
Rhode Island	18	8	20	0	0	0	0	0	0	0	0
Connecticut	65	11	50	0	0	0	0	0	0	0	1
MIDDLE ATLANTIC											
New York	238	100	332	11	9	0	1	2	0	0	6
New Jersey	153	58	113	0	0	0	0	2	0	0	3
Pennsylvania	205	103	243	0	0	0	0	0	0	0	2
EAST NORTH CENTRAL											
Ohio	201	59	190	0	0	0	0	0	0	0	2
Indiana	17	5	39	0	0	0	0	0	0	0	2
Illinois	22	21	114	5	1	0	1	0	2	0	6
Michigan [3]	72	65	196	0	4	0	1	0	0	0	14
Wisconsin	60	50	119	0	0	0	0	0	0	0	1
WEST NORTH CENTRAL											
Minnesota	9	23	41	0	0	1	0	0	0	0	5
Iowa	5	20	29	0	0	0	0	0	0	0	0
Missouri	19	8	16	0	0	2	0	0	0	0	2
North Dakota	5	2	3	0	0	0	0	0	0	0	0
South Dakota	6	2	2	0	0	0	0	0	0	0	0
Nebraska	12	18	18	0	0	0	1	0	0	0	0
Kansas	25	40	43	0	0	0	0	0	0	0	3
SOUTH ATLANTIC											
Delaware	2	0	1	0	0	0	0	0	0	0	0
Maryland [3]	65	22	112	0	0	0	0	2	0	0	1
District of Columbia	6	5	22	0	0	0	0	1	0	0	0
Virginia	47	62	62	0	0	16	0	0	1	0	1
West Virginia	17	6	35	0	0	0	0	0	0	0	0
North Carolina	160	159	159	0	0	0	0	0	0	3	0
South Carolina	92	73	73	3	15	0	0	0	0	1	0
Georgia	14	12	28	0	2	0	0	0	2	5	2
Florida	15	16	30	0	0	0	0	0	0	8	0
EAST SOUTH CENTRAL											
Kentucky	28	43	84	0	0	0	0	0	0	0	2
Tennessee	24	26	42	0	0	0	0	0	0	0	0
Alabama	22	10	18	5	0	0	0	0	0	4	3
Mississippi [3]				0	0	0	0	0	1	1	0
WEST SOUTH CENTRAL											
Arkansas	15	41	38	2	0	0	0	0	1	0	1
Louisiana	14	0	8	0	0	0	0	0	0	6	3
Oklahoma	8	1	36	0	1	0	0	0	0	1	0
Texas	391	316	318	12	326	55	0	0	1	32	17
MOUNTAIN											
Montana	16	4	5	0	0	0	0	0	0	0	0
Idaho	8	2	2	0	0	0	0	0	1	0	0
Wyoming	0	5	3	0	0	0	0	0	0	0	0
Colorado	15	25	25	0	0	0	0	0	0	0	0
New Mexico	14	17	33	0	0	0	0	0	0	0	0
Arizona	35	15	24	1	0	27	0	0	0	0	0
Utah	33	47	55	0	0	0	0	0	0	0	6
Nevada [3]	0	2	0	0	0	0	0	0	0	0	0
PACIFIC											
Washington	29	33	56	0	0	0	0	0	0	0	0
Oregon	19	30	28	0	0	0	0	1	0	0	7
California	425	98	375	1	3	0	0	0	0	0	6
Total	2,832	1,793	3,889	40	361	101	4	8	10	61	96
Same week 1944	1,793	------	------	21	323	107	21	5	9	46	------
Average 1942–44	3,254	------	------	24	193	69	14	[4]11	11	[4]20	------
17 weeks: 1945	42,080	------	------	482	7,463	1,976	114	16	285	822	1,466
1944	30,707	------	------	449	3,668	1,130	188	12	172	650	------
Average 1942–44	54,785	------	[4]65,384	416	2,699	843	168	[4]31	253	[4]626	------

[3] Period ended earlier than Saturday.

[4] 5-year median, 1940–44.

WEEKLY REPORTS FROM CITIES

City reports for week ended April 21, 1945

This table lists the reports from 90 cities of more than 10,000 population distributed throughout the United States, and represents a cross section of the current urban incidence of the diseases included in the table.

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
NEW ENGLAND												
Maine:												
Portland	0	0	------	0	1	0	4	0	2	0	1	1
New Hampshire:												
Concord	0	0	------	0	15	0	0	0	1	0	0	0
Vermont:												
Barre	0	0	------	0	1	0	1	0	1	0	0	0
Massachusetts:												
Boston	1	0	------	0	65	2	14	0	60	0	0	28
Fall River	0	0	------	0	1	0	1	0	2	0	0	1
Springfield	0	0	------	0	1	0	0	0	12	0	0	1
Worcester	0	0	------	0	2	0	13	0	16	0	0	5
Rhode Island:												
Providence	0	0	------	1	3	0	0	0	7	0	1	14
Connecticut:												
Bridgeport	0	0	------	0	0	0	2	0	4	0	0	0
Hartford	0	0	------	0	33	0	0	0	4	0	0	4
New Haven	0	0	------	0	1	1	0	0	2	0	0	7
MIDDLE ATLANTIC												
New York:												
Buffalo	0	0	------	1	3	0	7	0	8	0	0	3
New York	18	0	------	1	53	22	54	1	290	0	1	79
Rochester	0	0	------	0	23	1	3	0	13	0	0	14
Syracuse	0	0	------	0	1	0	2	0	2	0	0	22
New Jersey:												
Camden	1	0	3	1	2	1	2	0	1	0	0	1
Newark	0	0	1	0	3	0	3	0	19	0	0	6
Trenton	0	0	1	0	2	0	1	0	4	0	0	0
Pennsylvania:												
Philadelphia	3	0	1	0	168	2	40	0	76	0	1	76
Pittsburgh	0	0	------	0	5	3	11	0	40	0	0	16
Reading	0	0	------	0	2	1	1	0	9	0	0	0
EAST NORTH CENTRAL												
Ohio:												
Cincinnati	0	0	------	0	2	0	9	0	22	0	0	8
Cleveland	3	0	4	0	2	4	8	0	73	0	1	57
Columbus	0	0	------	0	2	0	3	0	5	0	0	2
Indiana:												
Fort Wayne	0	0	------	0	0	0	0	0	13	0	0	0
Indianapolis	3	0	------	1	6	0	6	0	18	0	0	2
South Bend	0	0	------	0	1	0	0	0	4	0	0	0
Terre Haute	0	0	------	0	1	0	1	0	2	0	0	0
Illinois:												
Chicago	1	0	2	1	104	6	26	0	132	0	0	21
Springfield	0	0	------	0	0	0	2	0	9	0	0	0
Michigan:												
Detroit	5	0	------	0	109	2	9	0	111	0	0	30
Flint	0	0	------	0	3	0	4	0	11	0	0	1
Grand Rapids	0	0	------	0	2	0	2	0	18	0	0	1
Wisconsin:												
Kenosha	0	0	------	0	0	0	0	0	2	0	0	2
Milwaukee	0	0	------	0	15	1	8	0	45	0	0	1
Racine	0	0	------	0	1	0	1	0	9	0	0	1
Superior	0	0	------	0	2	0	2	0	3	0	0	2
WEST NORTH CENTRAL												
Minnesota:												
Duluth	0	0	------	0	2	0	0	0	9	0	0	0
Minneapolis	0	0	------	0	4	1	0	0	20	0	0	3
St. Paul	0	0	------	0	4	0	2	0	7	0	0	0
Missouri:												
Kansas City	0	0	------	0	0	3	7	0	22	0	0	0
St. Joseph	0	0	------	0	2	0	0	0	19	0	0	0
St. Louis	2	0	5	0	6	5	6	0	33	0	3	14

City reports for week ended April 21, 1945—Continued

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
WEST NORTH CENTRAL—continued												
North Dakota:												
Fargo	0	0	------	0	1	0	1	0	2	0	0	0
Nebraska:												
Omaha	0	0	------	0	25	1	3	0	14	0	0	3
Kansas:												
Topeka	0	0	------	0	2	0	1	0	5	0	0	2
Wichita	1	0	------	0	3	0	1	0	5	0	0	9
SOUTH ATLANTIC												
Delaware:												
Wilmington	0	0	------	0	0	0	4	0	1	0	0	0
Maryland:												
Baltimore	5	0	1	1	15	5	9	0	77	0	2	70
Cumberland	0	0	------	0	0	0	1	0	4	0	0	0
Frederick	0	0	------	0	0	0	0	0	1	0	0	0
District of Columbia:												
Washington	1	0	------	0	12	3	10	0	36	0	1	9
Virginia:												
Lynchburg	0	0	------	0	5	0	2	0	3	0	0	2
Richmond	0	0	------	0	2	0	0	0	19	0	0	1
Roanoke	0	0	------	0	2	0	0	0	4	0	0	1
West Virginia:												
Charleston	0	0	------	0	0	0	0	0	1	0	0	0
Wheeling	0	1	------	0	20	0	0	0	0	0	0	4
North Carolina:												
Raleigh	0	0	------	0	19	0	2	0	1	0	0	14
Wilmington	0	0	------	0	2	0	1	0	0	0	0	3
Winston-Salem	0	0	------	0	0	0	1	0	3	0	0	0
South Carolina:												
Charleston	0	0	3	0	5	0	2	0	2	0	1	0
Georgia:												
Atlanta	0	0	3	0	1	0	2	0	12	0	0	1
Brunswick	0	0	------	0	3	0	3	0	0	0	0	4
Savannah	0	0	------	0	1	0	1	0	0	0	0	0
Florida:												
Tampa	0	0	------	0	1	0	5	0	1	0	0	5
EAST SOUTH CENTRAL												
Tennessee:												
Memphis	0	0	1	1	35	5	6	0	7	0	0	3
Nashville	0	0	------	1	0	0	3	0	7	0	1	0
Alabama:												
Birmingham	0	0	------	0	0	0	0	0	1	0	0	4
Mobile	0	0	------	0	0	0	2	0	1	0	0	0
WEST SOUTH CENTRAL												
Arkansas:												
Little Rock	0	0	------	0	1	0	2	0	0	0	0	1
Louisiana:												
New Orleans	3	0	------	0	26	3	5	1	2	0	1	2
Shreveport	0	0	------	0	0	0	3	0	0	0	0	0
Texas:												
Dallas	1	0	------	0	8	0	4	0	3	0	0	2
Galveston	0	0	------	0	0	0	1	0	2	0	0	0
Houston	1	0	------	0	0	0	2	1	2	0	0	0
San Antonio	1	0	------	1	4	0	5	0	0	0	0	2
MOUNTAIN												
Montana:												
Billings	0	0	------	0	1	0	0	0	4	0	1	0
Great Falls	0	0	------	0	0	0	1	0	2	0	0	2
Helena	0	0	------	0	0	0	0	0	0	0	0	0
Missoula	0	0	------	0	1	0	3	0	0	0	0	0
Idaho:												
Boise	0	0	------	0	0	0	1	0	0	0	0	0
Colorado:												
Denver	2	0	4	0	10	1	7	0	18	1	0	13
Pueblo	0	0	------	0	1	0	0	0	2	0	0	2
Utah:												
Salt Lake City	0	0	------	0	157	0	0	0	10	0	0	11

City reports for week ended April 21, 1945—Continued

	Diphtheria cases	Encephalitis, Infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
PACIFIC												
Washington:												
Seattle	0	0	-----	0	24	0	6	0	10	0	1	5
Spokane	3	0	2	2	1	0	3	0	3	0	0	0
Tacoma	0	0	-----	0	21	0	0	0	9	0	0	2
California:												
Los Angeles	1	0	2	1	83	2	6	0	61	0	0	39
Sacramento	0	0	-----	0	2	2	2	0	14	0	0	2
San Francisco	3	0	2	0	73	1	3	0	59	0	0	31
Total	59	1	35	13	1,220	78	369	3	1,558	1	16	672
Corresponding week, 1944	64	-----	59	32	7,184	-----	404	-----	2,257	0	10	277
Average, 1940–44	61	-----	117	[1] 31	[2] 6,763	-----	[1] 431	-----	1,755	2	14	996

[1] 3-year average, 1942–44. [2] 5-year median, 1940–44.

Dysentery, amebic.—Cases: New York, 3; Chicago, 1; Baltimore, 1.
Dysentery, bacillary.—Cases: Providence, 1; Buffalo, 1; New York, 2; Rochester, 1; Charleston, S. C., 4; Los Angeles, 3.
Dysentery, unspecified.—Cases: Cincinnati, 1; San Antonio, 33.
Leprosy.—Cases; Los Angeles, 1.
Typhus fever, endemic.—Cases: New York, 1; Chicago, 1 (1 death on April 15; infection acquired in Mexico, stated to be first case in Chicago since 1937); New Orleans, 2; San Antonio, 1.

Rates (annual basis) per 100,000 population, by geographic groups, for the 90 cities in the preceding table (estimated population, 1943, 34,394,800)

	Diphtheria case rates	Encephalitis, infectious, case rates	Influenza		Measles case rates	Meningitis, meningococcus, case rates	Pneumonia death rates	Poliomyelitis case rates	Scarlet fever case rates	Smallpox case rates	Typhoid and paratyphoid fever case rates	Whooping cough case rates
			Case rates	Death rates								
New England	2.6	0.0	0.0	2.6	322	7.8	91.5	0.0	290	0.0	5.2	159
Middle Atlantic	10.2	0.0	2.8	1.4	121	13.9	57.4	0.5	214	0.0	0.9	100
East North Central	7.3	0.0	3.6	1.2	152	7.9	49.3	0.0	290	0.0	0.6	78
West North Central	6.0	0.0	9.9	0.0	97	19.9	41.8	0.0	251	0.0	6.0	62
South Atlantic	9.8	1.6	11.4	1.6	144	13.1	70.3	0.0	270	0.0	6.5	186
East South Central	0.0	0.0	5.9	11.8	207	29.5	64.9	0.0	94	0.0	5.9	41
West South Central	17.2	0.0	0.0	2.9	112	8.6	63.1	5.7	26	0.0	2.9	20
Mountain	15.9	0.0	31.8	0.0	1,350	7.9	95.3	0.0	286	7.9	7.9	222
Pacific	11.1	0.0	9.5	4.7	323	7.9	31.6	0.0	247	0.0	1.6	125
Total	9.0	0.2	5.3	2.0	185	11.9	56.1	0.5	237	0.2	2.4	102

TERRITORIES AND POSSESSIONS

Virgin Islands of the United States

Notifiable diseases.—January–March 1945.—During the months of January, February, and March 1945, cases of certain notifiable diseases were reported in the Virgin Islands as follows:

Disease	January	February	March	Disease	January	February	March
Chickenpox	-----	2	1	Mumps	1	-----	-----
Filariasis	-----	2	-----	Poliomyelitis	-----	1	-----
German measles	1	-----	2	Schistosomiasis	-----	-----	1
Gonorrhea	6	15	9	Syphilis	8	11	7
Hookworm disease	3	-----	1	Tuberculosis (pulmonary)	1	1	3
Malaria	-----	-----	1	Typhus fever (murine)	3	1	-----
Measles	3	789	310	Vincent's angina	-----	-----	1

FOREIGN REPORTS

CANADA

Provinces—Communicable diseases—Week ended April 7, 1945.—During the week ended April 7, 1945, cases of certain communicable diseases were reported by the Dominion Bureau of Statistics of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Chickenpox		8		218	140	25	35	28	51	505
Diphtheria		2	1	28	3	2	1	4	1	42
Dysentery, bacillary				1						1
German measles		20		9	18			8	19	74
Influenza		30			83	2			28	143
Measles		3		80	82	11	26	26	241	469
Meningitis, meningococcus			1	1	1		1	1	1	6
Mumps		32		170	140	20	52	157	7	578
Poliomyelitis							2		1	3
Scarlet fever		3	9	59	49	17	5	21	19	182
Tuberculosis (all forms)		9	6	104	44	21	3	3	20	210
Typhoid and paratyphoid fever				10					2	12
Undulant fever				12	4					16
Venereal diseases:										
Gonorrhea	1	12	18	69	167	48	34	24	46	419
Syphilis		16	4	90	102	18	5	8	13	256
Other forms				1						1
Whooping cough		4		99	38	2	3	6	4	156

CUBA

Provinces—Notifiable diseases—4 weeks ended March 24, 1945.—During the 4 weeks ended March 24, 1945, cases of certain notifiable diseases were reported in the Provinces of Cuba as follows:

Disease	Pinar del Río	Habana [1]	Matanzas	Santa Clara	Camaguey	Oriente	Total
Cancer	2	1	9	5	2	12	31
Chickenpox		29	9	2	5	7	52
Diphtheria		21	4	1	1		27
Hookworm disease	14						14
Leprosy						2	2
Malaria	1	6	1	4	4	238	254
Measles		8	2	3	2	10	25
Poliomyelitis					1		1
Tuberculosis	9	28	31	24	5	55	152
Typhoid fever	10	59	11	20	14	41	155
Whooping cough				5			5
Yaws						1	1

[1] Includes the city of Habana.

GOLD COAST

Cerebrospinal meningitis.—Cerebrospinal meningitis has been reported in the colony of Gold Coast as follows: Week ended February 10, 1945, 525 cases with 93 deaths; week ended February 17, 1945, 826 cases with 91 deaths.

MAURITIUS

Poliomyelitis epidemic.—According to unofficial sources, an epidemic of poliomyelitis was reported on the island of Mauritius during March, with a total of 870 cases notified up to the end of the month. It was stated that assistance was being given by the officials of Kenya, Tanganyika, and Uganda, and that a physician and nurse had been sent to the island from England.

NEW ZEALAND

Notifiable diseases—4 weeks ended February 24, 1945.[1]—During the 4 weeks ended February 24, 1945, certain notifiable diseases were reported in New Zealand as follows:

Disease	Cases	Deaths	Disease	Cases	Deaths
Cerebrospinal meningitis	13	2	Scarlet fever	219	1
Diphtheria	61	3	Tetanus	1	----
Dysentery, bacillary	9	----	Tuberculosis (all forms)	160	46
Erysipelas	13	----	Typhoid fever	4	----
Malaria	15	----	Undulant fever	2	----
Puerperal fever	6	----			

REPORTS OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER RECEIVED DURING THE CURRENT WEEK

NOTE.—Except in cases of unusual incidence, only those places are included which had not previously reported any of the above-named diseases, except yellow fever, during the current year. All reports of yellow fever are published currently.

A table showing the accumulated figures for these diseases for the year to date is published in the PUBLIC HEALTH REPORTS for the last Friday of each month.

(Few reports are available from the invaded countries of Europe and other nations in war zones.)

Cholera

India—Calcutta.—Cholera has been reported in Calcutta, India, as follows: Week ended April 7, 1945, 294 cases, 90 deaths; week ended April 14, 1945, 452 cases, 148 deaths.

Plague

Morocco (French).—For the period April 1-10, 1945, 8 cases of plague were reported in French Morocco.

[1] No report was received for the week ended February 10, 1945.

Smallpox

British East Africa—Tanganyika.—For the week ended March 31, 1945, 510 cases of smallpox with 16 deaths were reported in Tanganyika, British East Africa.

Cameroon (French).—For the period March 21–31, 1945, 195 cases of smallpox were reported in French Cameroon.

French Guinea.—For the period April 1–10, 1945, 195 cases of smallpox were reported in French Guinea.

Nigeria.—For the week ended March 10, 1945, 302 cases of smallpox with 47 deaths were reported in Nigeria.

Sudan (French).—For the period April 1–10, 1945, 101 cases of smallpox were reported in French Sudan.

Union of South Africa.—For the month of January 1945, 394 cases of smallpox with 12 deaths were reported in the Union of South Africa.

Typhus Fever

Morocco (French).—For the period April 1–10, 1945, 558 cases of typhus fever (including 2 cases reported in Casablanca and 3 cases in Rabat) were reported in French Morocco.

Turkey.—For the week ended April 21, 1945, 86 cases of typhus fever (including 4 cases reported in Zonguldak, 1 case in Antalya, 1 case in Istanbul, and 1 case in Adana) were reported in Turkey.

Union of South Africa.—For the month of January 1945, 158 cases of typhus fever with 18 deaths were reported in the Union of South Africa.

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FEDERAL SECURITY AGENCY

UNITED STATES PUBLIC HEALTH SERVICE

THOMAS PARRAN, *Surgeon General*

DIVISION OF PUBLIC HEALTH METHODS

G. ST. J. PERROTT, *Chief of Division*

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